the long run include, myocardial infarction, stroke, renal failure, blindness, etc. Therefore, target values for biological markers have been determined below which organ damage does usually not occur and life expectancy is normalised. Examples for domains in which such thresholds have been defined are blood pressure, glycosylated haemoglobin (HbA1c), and others.
Inflammatory rheumatic diseases lead to organ damage not only in the musculoskeletal system but they may also harm internal organs. A target level of a measure related to its long-term outcome, can be a surrogate measure like the cholesterol level for cardiovascular diseases, or a composite measure of disease activity as used in RA (DAS28) or in AS (ASDAS). The treat-to-target strategy can be reduced to a simple algorithm of, on the one hand measuring activity and on the other hand, in consequence, adapting treatment. Treatment adaptation does not necessarily mean changing a medication or increasing the dosage of a drug but may even also mean life style changes, as long as the therapeutic target is attained or nearly attained - importantly within a prespecified time frame. Therapeutic adaptations should always take patient factors, including comorbidities, adverse events and patient preferences, into account.
However, the musculoskeletal system can mostly not be assessed by using a simple surrogate or direct “gold standard” measures, since rheumatic diseasese with multiple signs and symptoms are mostly rather complex. In RA information derived from physical examination using a quantitative joint count is considered very important. This is different in AS. Additionally, information from the history, which can be collected through patient self-report multifaceted questionnaires, has proven effective in determining patient status and its change. This is even more important in AS. However, functional impairment has reversible and irreversible components. Damage is a consequence of high and/or persisting disease activity. The most important variables contributing to joint damage in RA are swollen joint counts and C-reactive protein (CRP). The latter in combination with questions on back pain is also important in AS, while in RA the use of composite measures of disease activity that comprise joint counts is critical. There is good evidence that, if this strategy is consequently followed, physical function will improve and joint damage be reduced in patients with RA. To determine optimal treatment targets in RA it is necessary to define the thresholds of disease activity measures at which progression of joint destruction is halted. Of note, only remission is associated with maximal reversal of functional impairment and a stop of progression of damage as well as work disability. However, it needs to be realized that some remission criteria are more stringent than others.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7129

SP0055 WHAT ARE THE CHALLENGES FOR APPLYING TREAT TO TARGET IN AXIAL SPONDYLOARTHRITIS?

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The concept of Treat to Target (T2T) applied in rheumatoid arthritis has been evaluated in psoriatic arthritis and is currently under investigation in two different strategy trials in patients suffering from axial spondyloarthritis (axSpA). Whatever le results of these trials will be, the acceptation of this concept and consequently its implementation in daily practice might be challenging for several reasons.
The concept of T2T necessitates 3 different steps and also the close collaboration of the patient and the availability of different treatment modalities.
The three different steps consist in:
a) the choice of the most relevant outcome measure (e.g. a measure evaluating a domain recognized as predisposing to subsequent clinically relevant damage (either structural damage or important comorbidities such as cardiovascular diseases)).
b) the determination of the threshold of the outcome measure to reach (threshold below which the risk of subsequent damage is abolished or significantly decreased).
c) The time to reach the target is usually related to the treatment modality (a few days for NSAIDs and several weeks for DMARDs).
A part these different steps, two points have to be considered a) this T2T approach is impossible without embarking the patient in a true share decision b) this T2T strategy requires the possibility to adapt/increase the treatment in case the target is not reached after one or several “conventional” treatment modalities.
For each of these different points we will consider past-on ongoing initiatives proposing to resolve the different encountered issues in order to facilitate the elaboration and the implementation of a T2T strategy in AxSpA.
Disclosure of Interest: M. Dougados Grant/research support from: UCB,ABBVIE,PFIZER,MERCK, Consultant for: UCB,ABBVIE,PFIZER,MERCK
DOI: 10.1136/annrheumdis-2017-eular.7119

SP0056 UPDATE OF THE T2T RECOMMENDATIONS IN SPA

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In 2013 the first recommendations for treating spondyloarthritis to target (T2T) were published. These followed the reasoning for the T2T recommendations for rheumatoid arthritis. Although the systematic literature review at that time did not provide evidence to support the recommendations, five overarching principles and 11 recommendations were formulated. There were 9 commen recommendations for axial SpA, peripheral SpA and psoriatic arthritis and 2 additional recommendations for each subgroup specifically. In 2017 the T2T working group met again to update the recommendations. This was based on an updated systematic literature review. Data had been published that there is indeed a clear link between inflammation and subsequent longterm outcomes, which is the basis for the T2T principles.
SpA is characterised by musculoskeletal signs and symptoms (arthritis, enthesitis, dactylitis, axial disease) but also extra-articular manifestations (psoriasis, inflammatory bowel disease, anterior uveitis) are important manifestations. Moreover, comborbidities (such as osteoporosis, cardiovascular disease). All these manifestations are taken into account in the formulation of the recommendations. The overarching principles were kept largely identical. Some changes in the wording were made for a better understanding, but no fundamental changes were made. A total of 11 recommendations were formulated. These are now for all subgroups of SpA and no specific recommendations are proposed. In principle, the treatment target is remission or inactive disease of musculoskeletal and extra-articulaur manifestations, and the target should be individualised. It is important that remission/inactive disease should be based on a combination of clinical and laboratory parameters, and disease activity should be measured on the basis of clinical signs and symptoms as well as acute phase reactants. This is important to realise, e.g. in axial SpA as patient reported outcomes only are at best weakly correlated with structural damage. In certain circumstances, low disease activity may be an alternative target. Because of the heterogeneous presentation of SpA, not only the target, but also the assessments should be individualised. Both in the overarching principles and in the recommendation the shared decision between patient and rheumatologist is listed as the basis of the T2T management.
The updated recommendations will be presented.
Disclosure of Interest: D. Van Der Heijde Consultant for: AbbVie, Amgen, Astellas, AstraZeneca, BMS, Boehringer Ingelheim, Celgene, Daiichi, Eli-Lilly, Galapagos, Gilead, Janssen, Merck, Novartis, Pfizer, Regeneron, Roche, Sanofi, UCB, Employee of: Imaging Rheumatology
DOI: 10.1136/annrheumdis-2017-eular.7158

THURSDAY, 15 JUNE 2017

Calcium crystal deposition in rheumatic diseases —

SP0057 CALCIUM CRYSTALS AND THEIR LINK TO OSTEOARTHRITIS

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Calcification of cartilage is a common finding during osteoarthritis (OA). We have shown that it is mainly of the BCP type and not the CPPD type of crystal formation. BCP cartilage calcification is directly linked to the severity of cartilage degradation and, therefore, OA severity. We have also shown that with increasing hypertrophic differentiation of chondrocytes, the amount of calcification increases in vivo and in vitro. This indicates a link between chondrocyte hypertrophy andcartilage calcification. The pyrophosphate pathway is known to be involved in tissue calcification. It functions to keep the sensitive balance of pyrophosphate (PPi) and phosphate (Pi), thereby preventing the generation of calcium-phosphate crystals. One key player in this pathway is the nucleotide pyrophosphatase phosphodiesterase (NPP1), which has been demonstrated to be regulated by inflammatory mediators such as IL-1. In our cohort of OA patients, the expression of collagen X and NPP1, but not ANK and TNAP, correlated with cartilage calcification and also with the Mankin-Score. NPP1 expression inverse correlated with the calcification, whereas collagen X was upregulated. This finding was confirmed in experimental murine OA using the DMM mouse model. Furthermore, NPP1mut/mut mice (ttw/ttw) exhibit more calcification activity than wild type controls in joints as well as in cartilage of non weight bearing areas, including ear cartilage, suggesting that mechanical stress is not required for the induction of calcification. NPP1mut/mut (ttw/ttw) mice developed typical OA-like changes as evaluated by histological analysis as well as in vivo imaging and histological stainings. Intriguingly, calcification was associated with increased expression of the hypertrophic cartilage marker collagen X and the bone marker collagen I. Additionally, BCP crystals are able to activate chondrocyte differentiation via the WNT signaling pathway.
NPP1 is an important player in OA-associated cartilage calcification. Pathologic calcification of cartilage resembles in many aspects cartilage transformation into bone. Taken together, the data suggest that OA is characterized by the re-activation of molecular signalling cascades that at least in part resemble endochondral ossification.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7192

SP0058 REVIEW OF THE DIFFERENT IMAGING MODALITIES TO DETECT CALCIUM DEPOSITION DISEASES

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Crystal deposits in and around the joints are common and most often encountered

as incidental imaging findings in asymptomatic patients.
However, they can also cause chronic or acute arthropathy, generating symptoms. In the chronic setting, imaging features are usually characteristic and allow the differentiation of the type of crystal arthropathy. In the acute phase and in the early stages of the crystal deposition, the signs are often non-specific, and the final diagnosis still relies on the analysis of synovial fluid.
Radiography is the main imaging modality for the workup of these conditions. It can confirm the diagnosis and often characterizes the type of crystal arthropathy. In recent years, US has played an increasingly important role in this setting, and is a useful tool in superficially located crystal-induced arthropathies. CT nicely complements radiography for deeper sites, especially the axial skeleton. DECT is a promising tool for the characterization of crystal arthropathies, in particular gout as it permits a quantitative assessment of deposits, and may help in the follow up of patients.
When performed in the acute stage, MRI may show severe inflammatory changes that could be misleading and correlation to radiographs or CT should help to distinguish crystal arthropathies from infectious or tumoral conditions.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7263

THURSDAY, 15 JUNE 2017

Fifty shades of remission in RA

SP0059 REMISSION: MORE THAN CLINICAL ...?

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This session is about defining remission. Most examples will be about rheumatoid arthritis (RA) because most experience has been gathered in that disease. But the concept of remission should be viewed from a wider perspective than one disease. The session includes two pro-con debates (on the utility of including imaging and biomarkers in a definition of remission).
As in all things, when embarking on a scientific project, one must ask:
"Why are we doing this?"
To even begin with answering the question, we must first agree on a clear conceptual definition of remission. When we started on the development of the ACR-EULAR definition of remission in RA, we used dictionary sources and discussions to settle on this:
"The state of absence of disease activity in patients with a chronic illness, with the possibility of return of disease activity." [1]
It is clear that choices are made from the beginning, especially with the concept "disease activity", and the possibility that disease activity returns (as opposed to "healing", where this possibility does not exist). Disease activity is a tangible concept adequately defined in RA, but less so in many other rheumatological diseases. Also, disease activity is conceptually separate from (mostly irreversible) consequences of the disease, such as damage. Finally, note that the above concept does not contain the elements "duration" or "treatment".
If we continue with the above concept, why do we want to proceed to operationalize the remission definition? The two main reasons are research and patient care. For both, it is clear that we are defining a very good, perhaps even the best state a patient can be in, given that we are talking about chronic disease, i.e. the root cause of the disease cannot be taken away to heal the patient. Being in such a good state has immediate benefits (minimal disease impact) and probably also future benefits, if lack of disease activity translates to less consequences (damage etc). In both research and patient care, we want a definition that is both valid (favorable test characteristics; links to prognosis) and feasible (time, costs, interpretability). Validity and feasibility oppose each other to a certain extent (eg, definitions with better sensitivity and specificity are usually more expensive). Research and patient care differ in their use of the definition. In research, validity and feasibility can be lower than in patient care, because research is about groups, and cost and interpretability are less of an issue than in patient care.
Most of the people criticizing the current ACR-EULAR remission definition of RA are confused over its purpose: whereas it was intended for use in trials, they criticize it for lack of validity in the clinic. For instance, it is felt that the patient global criterion is too strict, so that patients with no apparent inflammatory activity but a patient global score of 2 or higher (scale 0–10) are "unjustly" not classified as in remission. Also, the lack of a duration or treatment criterion is felt to be a problem, but this is not an issue in research.
In the following pro-con debates, please consider the following:
Proposals to change existing criteria for remission must also be held to the question: "Why are we doing this?"
References:
[1] Remission. (Accessed 21–02–2017, at http://en.wikipedia.org/wiki/Remission.)
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7124

SP0060 BIOMARKERS ARE REQUIRED FOR REMISSION: PRO

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1. Conceptually, remission is thought of as a state where the disease is absent. As we approach a better understanding of the underlying pathophysiological process of a disease, it becomes more and more relevant to include in a definition of remission appropriate biochemical markers of that process.
2. From a practical point of view, definitions of remission in RA have been built upon clinical parameters of disease activity, supplemented in some cases with a single biomarker. However, it is clear that in practice these definitions are insufficiently precise: held against a gold standard of expert opinion, they perform at around 80–90%, misidentifying one or two out of every ten patients. And while there is an understandable and in many ways desiriable development of more patient-reported emphasis in outcomes, it has considerable practical value to be able to objectify an important disease state such as remission.
3. There is convincing evidence to show that biomarkers can be employed succesfully to predict some aspects of RA. In the day-to-day care of patients with this disease, the most important prediction may be whether the effective drug can be tapered or not. Current evidence indicates that biomarkers may be invaluable at helping clinicians and their patients make this important decision.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7288

THURSDAY, 15 JUNE 2017

Innate immunity

SP0061 A DAY IN THE NEUTROPHIL'S LIFE

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Immunity is essential for life, yet the strength of immune responses are not constant throughout the day. This oscillatory immunity reflects an adaptation of organisms to environmental changes that occur through day-night cycles, so as to optimize and concentrate effective responses to the times of maximal environmental threat. In my talk I will discuss our ongoing efforts to uncover the mechanisms by which neutrophils, the most abundant and aggressive of all immune cells, orchestrate temporal immunity. These mechanisms are reflected in diurnal changes in phenotype and function of neutrophils, which we refer to as neutrophil aging. We propose that the existence of a timed response of neutrophils governed by cell-intrinsic and –extrinsic mechanisms suggests that inflammatory disease co-opts ancestral processes to damage tissues.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7054

SP0062 DIFFERENTIAL SCAVENGING OF APOPTOTIC CELLS AND BACTERIA

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During inflammation and infection, we are simultaneously confronted with both self and non-self in form of dying cells and microbes, respectively. Mechanisms that facilitate the non-immunogenic clearance of self-antigens derived from apoptotic and necrotic cells and that, in parallel, allow the initiation of an immune response against invading pathogens are incompletely understood. Recent data from our laboratory show that the immune system actively sorts apoptotic cells (ACs) and bacteria into distinct subspecies of phagocytes thereby enabling a segregated processing of self and non-self as well as a differential immune response against these two entities. During inflammation, ACs were cleared by tissue resident macrophages (resMφ) that performed a non-immunogenic disposal of self antigens, whereas bacteria were preferentially ingested by monocyte-derived inflammatory macrophages. We identified the enzyme 12/15-lipoxygenase and the nuclear receptor Nr4a1, both specifically expressed by resMφ, as key factors that control the coordinated and non-immunogenic phagocytosis of ACs by these specialized macrophage subset. Incorrect sorting and aberrant uptake of AC-derived self-antigens by pro-inflammatory and immunocompetent phagocytes, however, resulted in the break of self-tolerance and autoimmunity. Our data thus demonstrate the importance of a sorted clearance of ACs for the maintenance of immunologic self-tolerance.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7198

SP0063 THE ROLE OF MUSCLE IN INNATE IMMUNE RESPONSES

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The skeletal muscle represents a unique site from the immunological point of view. Leukocytes are virtually absent in healthy conditions. However they are quickly recruited upon muscle injury, persist during the regenerative phases to disappear again after tissue healing. Thus, it represents and ideal scenario to study the